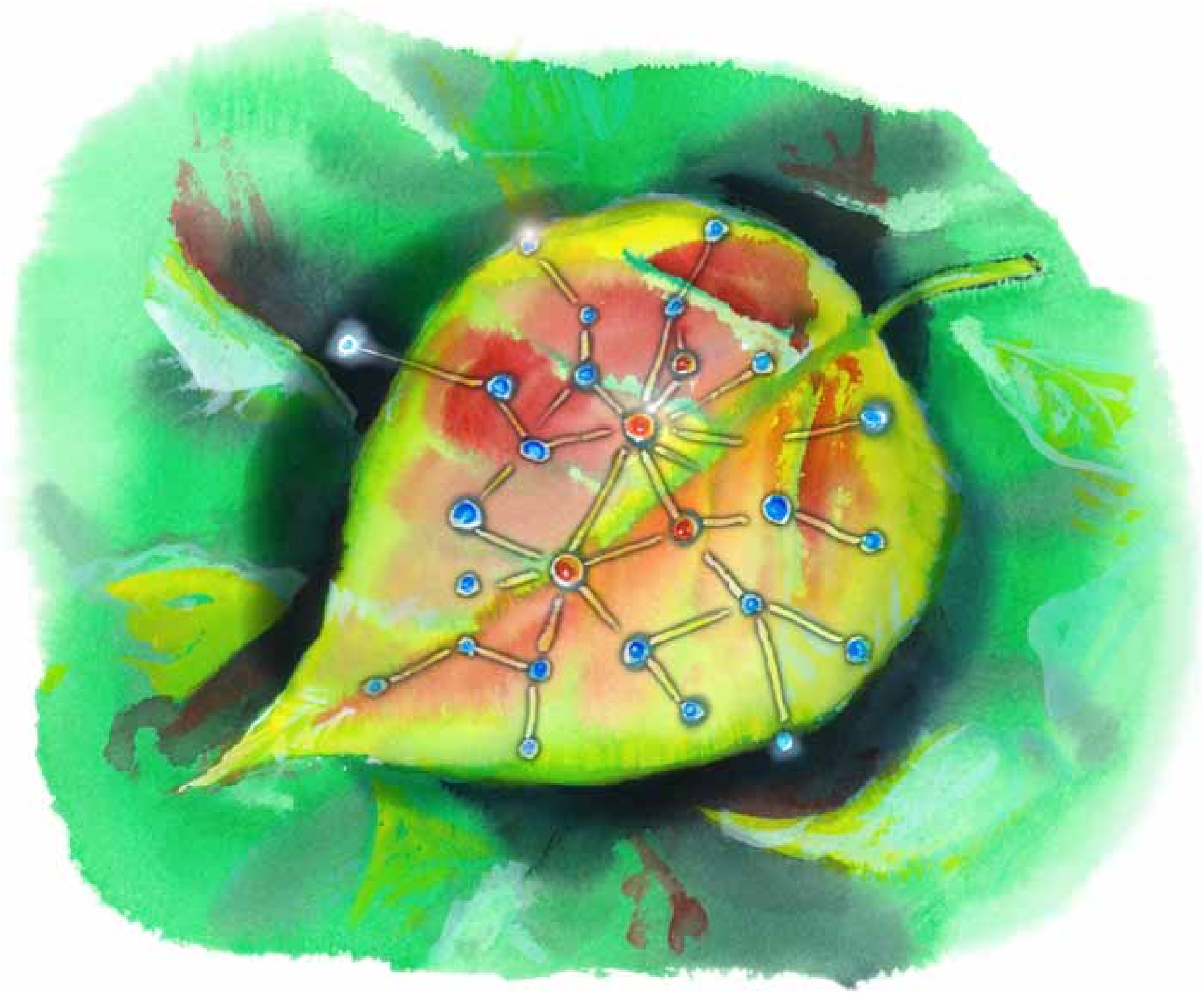
15th *New Phytologist* Symposium

Networks in Plant Biology

The Linnean Society
London, UK
26-27 January 2006



Programme, abstracts & participants

New Phytologist

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Organizing Committee

Claire Grierson (*University of Bristol, UK*)
Alistair Hetherington (*Lancaster University, UK)*
Andrew Millar (*University of Edinburgh, UK)*
Holly Slater (New Phytologist, *Lancaster, UK)*
Ian Woodward (*University of Sheffield, UK*)

Acknowledgments

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Programme, abstracts and participant list compiled by Helen Pinfield-Wells and Jayne Young.
Networks illustration by Sam Day, www.samday.com

Programme

Thursday 26 January

12:00–13:00	Registration & lunch
13:00	**Welcome & introductions**, Alistair Hetherington

Session I

Chairperson: Andrew Millar

13:00–13:40	**David Fell**, Oxford Brookes University, UK Perspectives on genomic scale metabolic networks
13:40–14:20	**Lee Sweetlove**, University of Oxford, UK Getting to grips with the metabolic network
14:20-15:00	**Claire Grierson**, University of Bristol, UK Towards the molecular network that underlies polarised growth
15:00–15:30	Refreshment break
15:30–16:10	**Nick Monk**, University of Sheffield, UK Using mathematical models as tools to probe biological networks
16:10–16:50	**Andrew Millar**, University of Edinburgh, UK Modelling and analysis of the clock gene network
16:50–17:30	**John Turner**, University of East Anglia, UK Stress signals
17:30-18:30	Reception

Friday 27January

Session II
Chairperson: Claire Grierson

09:30–10:10	**Hamid Bolouri**, Institute for Systems Biology, Seattle, USA A computational tool set for modelling developmental genetic regulatory networks
10:10–10:50	**Juliette Colinas**, Duke University, Durham, USA Studying transcription factor networks in root development: a genomics approach
10:50–11:20	Refreshment break
11:20–12:00	**Ian Woodward**, University of Sheffield, UK Stomatal networks: from leaf to globe
12:00–12:40	**Jane Memmott**, University of Bristol, UK Plants as members of ecological communities: their links with the real world
12:40-13:20	**Andrew Bangham**, University of East Anglia, UK Measuring and modelling shape
13:20- 13:30	Concluding remarks – Ian Woodward
13:30–14:15	Lunch and depart

Speaker Abstracts

Perspectives on genomic scale metabolic networks

DAVID FELL
School of Biological & Molecular Sciences, Oxford Brookes University, Oxford, OX3 0BP, UK

The increasing availability of annotated genome sequences raises the question of the extent to which it is possible to reconstruct the metabolic phenotype from such data. The first stage is to convert the annotation into a consistent and connected model of the corresponding metabolic network. Some of the difficulties that arise at this stage, even with microbial genomes, will be illustrated, and the further challenges in interpreting plant genomes discussed. The next step is analysis of the structure of the network, using a variety of techniques that can predict such things as pathways through the network, and their stoichiometric yields. Examples will be given where elementary modes analysis has predicted unexpected routes through the network, though it, like several other approaches, is more readily applied to portions of the network than to entire genomic scale models. Enzyme subsets analysis shows small clusters of enzymes that must always function together, and examples will be given to show that the enzymes in a subset frequently show strong correlations in transcriptome analysis.

Getting to grips with the metabolic network

LEE SWEETLOVE
Department of Plant Sciences, University of Oxford, South Parks Road, Oxford, OX1 3RB, UK

Of all the molecular-interaction networks in plants, metabolism is by far and away the most completely described both in terms of network topology and in terms of the properties of its molecular components. Moreover, experimental tools now exist that allow systematic measurement of its behaviour. The construction of a mathematical model that encapsulates the metabolic network of plants at 'genome scale' is therefore a plausible goal (especially in the case of model plants such as Arabidopsis). However, although genomic information provides a starting point in establishing a consensus metabolic network topology, a great deal of experimental input will also be required. This will include transcriptomic / proteomic data to constrain the model to those enzymes actually present under a given condition as well as metabolic flux maps to validate the model output. The importance of the integration of experimental data into models will be discussed and examples will be given to show how different experimental strategies can be used to provide information about the regulatory structure within the metabolic network.

Towards the molecular network that underlies polarised growth

CLAIRE GRIERSON
School of Biological Sciences, University of Bristol, BS8 1UG, UK

Many important specialised structures, such as pollen tubes and root hairs in plants, and sensory nerve cells in animals, are produced by polar cell growth. Molecular genetic and genomic studies are revealing that at least some of the machinery that drives polar growth is conserved across eukaryotes. We are identifying this machinery in root hair cells, and, using comparative genomics, in other cell types.

We are also beginning to consider the conceptual and technical challenges that must be met if we are to successfully model mechanisms of polar growth in plants.

Using mathematical models as tools to probe biological networks

NICK MONK
*Department of Computer Science, University of Sheffield, Regent Court, 211 Portobello Street,
Sheffield, S1 4DP, UK*

Emerging technologies are contributing to a rapid growth in our ability to elucidate the topological structure of large regulatory networks. While network topology is of clearly of great importance, it is the dynamical behaviour of a network that determines the nature of the related biological process. Understanding of dynamics requires knowledge of the form of functional interactions between network components, and the acquisition of these data is often the rate-limiting step in attempts to determine network dynamics. I will discuss how mathematical models of regulatory networks can be used to direct functional studies by identifying putative key network interactions on which to focus experimental attention. The iterative use of complementary modelling and functional studies can thus be used as a tool to uncover the core regulatory logic of biological networks.

Modelling and analysis of the clock gene network

ANDREW MILLAR
University of Edinburgh, Institute of Molecular Plant Sciences, Mayfield Road, Edinburgh, EH9 3JH, UK

Eukaryotes and some prokaryotes have adapted to the 24h day/night cycle by evolving circadian clocks. The circadian clock now controls 24-hour rhythms in very many aspects of metabolism, physiology and behaviour. Day-length (photoperiod) measurement depends on the circadian clock, so the 24h clock mechanism also governs seasonal rhythms, such as reproduction. In the model plant species, *Arabidopsis thaliana*, the clock controls the expression of at least 12% of genes at the RNA level (Edwards et al. 2005), and this proportion is similar in other eukaryotes. Fundamental properties of the clock are shared across taxonomic groups, such as phase resetting by light signals and temperature compensation of the circadian period.

All the known clock mechanisms include a gene circuit with negative feedback, involving 24h rhythms in the levels of positive- and negatively-acting transcriptional regulators (Young and Kay, 2001). Molecular genetics has identified 5-20 genes that are involved in constructing these regulatory loops in cyanobacteria, Drosophila, Neurospora, Arabidopsis and mouse. Other components almost certainly remain to be discovered and each oscillator may involve multiple feedback loops, some with different biochemical mechanisms. Strikingly, the protein sequences of the clock components are distinct to each taxonomic group, suggesting that clocks may have evolved several times. Some features of the regulatory circuits are shared among groups, suggesting that the circuit architecture may be important for clock function. Circadian regulation is ubiquitous, pervasive and has complex properties, yet the number of components in the clock is relatively small, making this an excellent prototype for reverse engineering of a genetic sub-network.

My experimental group has previously identified new components of the plant circadian clock, using the bioluminescent reporter gene luciferase (*LUC*) to reveal gene expression rhythms with high spatial and temporal resolution. As the details revealed by molecular genetics do not necessarily lead to greater understanding of a regulatory circuit, we have also developed differential equation models for the plant clock and photoperiod sensor, together with our collaborators in IPCR. The models incorporate molecular components in a realistic manner, so numerical simulations using the models are now directing the design and evaluation of molecular experiments (Goldbeter, 2002). Experiments designed to test a prediction of our circadian clock model recently led us to identify *GIGANTEA* in a new location of the clock network (Locke et al, 2005b). We are now extending this work to include further components of the clock gene circuit. We developed Circadian Modelling, an experimentalist-friendly interface for the models, to allow other groups to explore alternative experimental designs rapidly (free online at http://www.amillar.org/Downloads.html). David Rand and colleagues have established a novel analytical method to assess the contribution of each component of the model (RNA or protein) at each phase of the cycle (Rand et al, 2004). This work indicates a general explanation for the evolution of multi-loop structures, to allow flexible regulation, providing one of the design principles that may underlie the architecture of all circadian clock gene circuits. Funded by BBSRC, EPSRC and DTI.

References

Young MW, Kay SA. 2001. Time zones: A comparative genetics of circadian clocks. *Nature Reviews Genetics* **2:** 702-715.

Goldbeter A. 2002. Computational approaches to cellular rhythms. *Nature* **420:** 238-245.

Rand DA, Shulgin BV, Salazar D, Millar AJ. 2004. Design principles underlying circadian clocks. *Journal of the Royal Society Interface* **1:** 119-130.

Locke JC, Millar AJ, Turner, MS. 2005a. Modelling genetic networks with noisy and varied experimental data: the circadian clock in *Arabidopsis thaliana*. *Journal of Theoretical Biology* **234:** 383-393.

Locke JCW, Southern MM, Kozma-Bognar L. Hibberd V, Brown PE, Turner MS, Millar AJ. 2005b. Extension of a genetic network model by iterative experimentation and mathematical analysis. *Molecular Systems Biology*, doi: 10.1038/msb4100018.
Edwards KD, Anderson PE, Hall A, Salathia NS, Locke JCW, Lynne JR, Straume M, Smith JQ, Millar AJ. 2005. FLOWERING LOCUS C mediates natural variation in the high temperature response of the Arabidopsis circadian clock. *The Plant Cell* in press

Stress signals

JOHN TURNER
School of Biological Sciences, University of East Anglia, Norwich Research Park, Norwich, NR4 7TJ, UK

Arabidopsis plants respond to environmental stress through adaptive responses that modify patterns of gene expression, biochemical pathways, physiological responses, growth rate, and architecture. We have developed a model stress – response pathway in which a stress (wounding) and the response (activation of a the jasmonate-responsive promoter of the vegetative storage protein gene VSP1) is used to identify mutations that alter the response, and to identify inputs from other signal pathways that moderate this response. New data is presented that reveals integrated regulation of the stress-response pathway at the level of transcription, RNA-processing, and protein processing. Models are presented that simulate the pathway, and its interaction with outputs from other signal pathways.

A computational tool set for modelling developmental genetic regulatory networks

HAMID BOLOURI
Institute for Systems Biology, Seattle, WA 98103-8904, USA

Developmental genetic regulatory networks (GRNs) have unique architectural characteristics. They are typically large-scale, multi-layered, and organized in a nested, modular hierarchy of regulatory network kernels, function-specific building blocks, and structural gene batteries. They are also inherently multicellular and involve changing topological relationships among a growing number of cells. Reconstruction of developmental GRNs requires unique computational tools that support the above representational requirements. In addition, I argue that DNA-centered network modeling, separate descriptions of network organization and network behavior, and support for network documentation and annotation are essential requirements for computational modeling of developmental GRNs. Based on these observations, we have developed a number of freely available, platform-independent, Open Source software packages which support both the process of model construction, and also model visualization, analysis, documentation, and dissemination. I will provide an overview of the main features of these tools and recommend them as substrates for further co-development for and by the developmental biology community.

Studying transcription factor networks in root development: a genomic approach

JULIETTE COLINAS
Biology Department, Box 91000, Duke University, Durham, NC 27708, USA

We wish to identify the transcriptional networks that regulate plant development using high through-put techniques. For this we need global expression profiles at cell-type specific resolution and direct transcription factor DNA binding data at different stages of development. The Arabidopsis root is particularly well-suited to obtain these data, as it is radially symmetric and develops continuously from a set of stem cells in its tip. This results in different developmental stages being located along its longitudinal axis. We have developed a method to determine global expression patterns at cell-type specific resolution. We have generated a map of gene expression for many of the cell types including the stem cells in the root of Arabidopsis. From this dataset we have identified transcription factors with tissue-specific expression in the root. We have made transcriptional and translational fusions of these transcription factors to GFP and introduced them into plants. The resulting expression patterns were analyzed to improve the expression map, identify regulatory regions responsible for tissue-specific expression, and determine when transcription factors move intercellularly. In a complementary project we are using convergent genomics approaches to identify the targets of transcription factors that control stem cell identity and radial patterning.

Stomatal networks: from leaf to globe

IAN WOODWARD
Department of Animal and Plant Sciences, University of Sheffield, Western Bank, Seffield, S10 2TN, UK

All controls of stomata translate to either variations in number or variations in opening. Globally the combined effects of opening and number control the transpiration of $30*10^{18}$ g of water vapour and the inward and outward exchange of 10^{18} g of carbon dioxide. Such large exchanges directly influence climate as well as the growth and development of vegetation. It is no surprise therefore that there are complex controls of stomatal behaviour and development. New developments are starting to unravel the network of processes internal and external to the plant that influence stomata. One example to be described is the effect of changing carbon dioxide concentration on stomata. The carbon dioxide effect has typically been considered in terms of either an impact on opening or on stomatal development. However there is evidence that links both features. In addition there is no obvious carbon dioxide detector for development – rather the response hijacks the plant defence network. The impacts of these carbon dioxide responses are considered, finally, at the global scale.

Plants as members of ecological communities: their links with the real world

JANE MEMMOTT
School of Biological Sciences, University of Bristol, Woodland Road, Bristol, BS8 1UG, UK

Under natural circumstances plants interact with a large number of other species. For example they are eaten by herbivores, their flowers are visited by pollinators and their seeds are spread by seed dispersers. Given that many of these interactions will be generalized, interactions between plants and other species will be embedded in a complex network of biotic interactions. In this talk I will discuss the structure and function of these networks, looking at patterns of specialisation and at responses to environmental variation.

Measuring and modelling shape

ANDREW BANGHAM
School of Computing Sciences, University of East Anglia, Norwich, NR4 7TJ, UK

The shape of organs establishes a spatial context in which gene networks operate. In different contexts networks behave differently and contribute differently to survival. Shape can be quantified using principal components analysis. For example, used to quantify leaf shape it provides correlates for QTL analysis allowing each genetic locus to be represented in the resulting allometric space. It does not, however, provide a mechanistic understanding of how shapes develop. At a high level, growth in two dimensions can be modelled using geometric meshes such as networks of springs or finite element models. The difficulty lies in measuring the growth parameters. Natural or artificial features can be tracked to produce growth parameters directly. Clonal analysis requires a geometric mesh model to infer the pattern of growth from adult petals. Given spatial models of growing organs and classical L-system models for representing the branching structure of plants, plants provide the first opportunity to develop models for indexing spatiotemporal experimental data, including network behaviour, on growing systems.

Participants

Participant	Establishment	Country	Email	Research interests
Amtmann, Anna	University of Glasgow	UK	a.amtmann@bio.gla.ac.uk	Ion transport, mineral nutrition, salt tolerance, transcriptomics, metabolomics, signalling, systems biology
Anfodillo, Tommaso	University of Padova	Italy	tommaso.anfodillo@unipid.it	Xylem structure, conduit tapering, maximum tree height, treeline
Armengaud, Patrick	University of Glasgow	UK	p.armengaud@bio.gla.ac.uk	Potassium, Nutrition, Transcriptome, Metabolome, Signaling, Transduction, abiotic stress, biotic stress
Baker, Neil	University of Essex	UK	baken@essex.ac.uk	Photosynthesis, environmental stress, electron transport, chlorophyll fluorescence, signalling
Bangham, Andrew	University of East Anglia	UK	ab@cmp.uea.ac.uk	See abstract
Barker, Guy	University of Warwick	UK	guy.barker@warwick.hri.ac.uk	Genomics, comparative, genetics, pathways, oils, fatty acid, embryogenesis, EST, sequence, analysis
Bastow, Ruth	Unversity of Bristol	UK	ruth@arabidopsis.info	Community, co-ordination, dissemination, genomics, liaison, out-reach, resources, technology
Bebber, Daniel	University of Oxford	UK	dan.bebber@plants.ox.ac.uk	Ecology, statistics, networks, fungi, forests, nutrient cycling
Bennett, Malcolm	University of Nottingham	UK	malcolm.bennett@nottingham.ac.uk	Arabidopsis, auxin transport, root development, lateral root development, plant hormones, cell division, cell expansion, mathematical modelling
Bogre, Laszlo	Royal Holloway, University of London	UK	l.bogre@rhul.ac.uk	Cell cycle, growth, signalling pathways, MAP kinases, transcriptomics, metabolomics
Bolouri, Hamid	Institute for Systems Biology	USA	hbolouri@systemsbiology.org	See abstract
Breen, Gordon	University of Bristol	UK	gordon.breen@bris.ac.uk	root hairs, bioinformatics, molecular networks, polar growth, microarrays
Broadley, Martin	University of Nottingham	UK	martin.broadley@nottingham.ac.uk	plant mineral nutrition
Buchanan-Wollaston, Vicky	University of Warwick	UK	vicky.b-wollaston@warwick.ac.uk	Arabidopsis, functional genomics, leaf senescence, signalling networks, regulation, gene expression
Colinas, Juliette	Duke University	USA	Jhc16@duke.edu	See abstract
Correa, Luiz	Potsdam University	Germany	correa@uni-potsdam.de	Transcription factors, phylogeny, regulation, DNA binding, cascade, network, expression pattern, repression
Desikan, Radhika	University of the West of England	UK	radhika.desikan@uwe.ac.uk	Reactive oxygen species, nitric oxide, stomata, abiotic and biotic stress, defence, sensing and signalling
Fell, David	Oxford Brookes University	UK	dfell@brookes.ac.uk	See abstract
Fleming, Andrew	University of Sheffield	UK	a.fleming@sheffield.ac.uk	Development, cell cycle, cell wall, leaf, meristem
Fricker, Mark	University of Oxford	UK	mark.fricker@plants.ox.ac.uk	Fungal networks, stomatal physiology, signal transduction, amino acid transport, confocal imaging, glutathione, calcium, pH
Garibaldi, Jon	University of Nottingham	UK	jmg@cs.nott.ac.uk	Computer modelling, model optimisation, heuristics, decision support, uncertainty handling
Gay, Alan	IGER	UK	alan.gay@bbsrc.ac.uk	Plant Physiology, Crop Physiology, Hyperspectral measurements on plants, Multivariate Analyses, Modelling cold hardening, Breeding for Stomatal control, Photosynthesis
Gilmartin, Philip	University of Leeds	UK	n.m.hutchinson@leeds.ac.uk	
Gray, Julie	University of Sheffield	UK	j.e.gray@sheffield.ac.uk	Arabidopsis, cell signalling, abiotic stress, guard cells, germination
Green, Rachel	Hebrew University	Israel	rgreen@vms.huji.ac.il	Arabidopsis, genes, circadian, flowering, genomic, clock
Grierson, Claire	University of Bristol	UK	claire.grierson@bristol.ac.uk	See abstract
Hetherington, Alistair	Lancaster University	UK	a.hetherington@lancaster.ac.uk	
Hodgman, Charlie	University of Nottingham	UK	Charlie.Hodgman@nottingham.ac.uk	Systems biology, root development, integrative biology, bioengineering, bioinformatics
Holdsworth, Michael	University of Nottingham	UK	michael.holdsworth@nottingham.ac.uk	Germination, network regulation of plant development, crop genetics, developmental biology, transcription factor function, metabolic control of development
Jackson, Stephen	Warwick University	UK	stephen.jackson@warwick.ac.uk	Flowering, Photoperiod, Systems biology, Stature, Hormone response
Jensen, Oliver	University of Nottingham	UK	oliver.jensen@nottingham.ac.uk	Mathematical, modelling, biology, medicine, biomechamics
Jiang, Kun	Lancaster University	UK	daisy1684@hotmail.com	Guard cell, transcription factor signal transduction, network

Jones, Jonathan	John Innes Centre	UK	jonathan.jones@sainsbury-laboratory.ac.uk	
Kepinski, Stefan	University of York	UK	ssk2@york.ac.uk	Plant hormones, modelling, shoot branching
King, John	University of Nottingham	UK	john.king@nottingham.ac.uk	Mathematical modelling, systems biology nonlinear systems, cell signalling multiscale modelling tissue mechanics
Knight, Marc	University of Oxford	UK	marc.knight@plants.ox.ac.uk	Abiotic stress, biotic stress, signalling, calcium, reactive oxygen species, gene expression
Lake, Janice	University of Sheffield	UK	j.a.lake@sheffield.ac.uk	Stress, signalling, networks, physiology, stomata
Liang, Yun-Kuan	Lancaster University	UK	y.liang5@lancaster.ac.uk	Signal transduction, Guard cell, Gene regulation, Plant development
Lindsey, Keith	University of Durham	UK	keith.lindsey@durham.ac.uk	
Lopez-Juez, Enrique	Royal Holloway, University of London	UK	e.lopez@rhul.ac.uk	Photobiology, chloroplast biogenesis, leaf development, plastid signalling, transcriptomics
Love, John	University of Exeter	UK	J.Love@exeter.ac.uk	Calcium, photoperiodism, signalling networks
May, Sean	NASC / University of Nottingham	UK	sean@arabidopsis.info	Bioinformatics, transcriptomics, germplasm
Memmott, Jane	University of Bristol	UK	Jane.memmott@bristol.ac.uk	See abstract
Millar, Andrew	University of Edinburgh	UK	Andrew.millar@ed.ac.uk	See abstract
Monk, Nick	University of Sheffield	UK	n.monk@sheffield.ac.uk	See abstract
Mullineaux, Phil	University of Essex	UK	mullin@essex.ac.uk	Redox control, signalling, abiotic stress, reactive oxygen species, oxidative stress, water relations, drought, photosynthesis
Murao, Taro	University of Newcastle upon Tyne	UK	Taro.Murao@ncl.ac.uk	Mathematical biology, developmental biology, pattern formation, morphogenesis, neuroscience
Ongaro, Veronica	University of York	UK	vo100@york.ac.uk	Shoot branching, plant hormones, L-system, biological modelling, plant development
Owen, Marcus	University of Nottingham	UK	markus.owen@nottingham.ac.uk	Mathematical biology, developmental biology, pattern formation, morphogenesis, neuroscience
Panagopulos, Michael	Lancaster University	UK	m.panagopulos@lancs.ac.uk	Stomata, guard cells, networks, modelling, statistics, microarry, signal transduction
Petit, Giai	University of Padua	Italy	giai.petit@unipd.it	Xylem anatomy, network models, plant physiology, tree growth, ecology
Pinfield-Wells, Helen	New Phytologist	UK	h.pinfield-wells@lancaster.ac.uk	Organizer
Roberts, Desmond	HRI Wellesborne	UK	D.Roberts@theboggygarden.fsnet.co.uk	Virtual environment simulation, 3-D graphics, fractal dimensions, clusters, lacunarity, ecological systems, spatial dynamics, temporal dynamics, plant canopy effects, graphical modelling
Roberts, Irene	HRI Wellesborne	UK	I.J.Roberts@warwick.ac.uk	Biological control, canopy structure, predator behaviour, lacunarity, fractal dimensions, computer simulations, spatial dynamics, individual-based modelling, pest aggregation, canopy effects on biodiversity"
Robson, Fran	University of East Anglia	UK	F.Robson@uea.ac.uk	Arabidopsis, genetics, jasmonate, light, stress, abiotic/biotic, signalling, hormone, molecular, development
Shanahan, Hugh	Royal Holloway, University of London	UK	Hugh.Shanahan@rhul.ac.uk	Protein-DNA, interactions, solubility, structure, machine learning, statistics
Skirycz, Aleksandra	University of Potsdam	Germany	skirycz@mpimp-golm.mpg.de	Leaf growth, biomass accumulation, transcription factors, signal transduction, abiotic stress
Slater, Holly	New Phytologist	UK	h.slater@lancaster.ac.uk	Organizer
Surridge, Christopher	Public Library of Science	UK	csurridge@plos.org	Surridge, Christopher
Sweetlove, Lee	University of Oxford	UK	lee.sweetlove@plant-sciences.ox.ac.uk	See abstract
Tansley, Geoff	University of Nottingham	UK	geoff.tansley@nottingham.ac.uk	
Thompson, David Stuart	University of Westminster	UK	thompss@wmin.ac.uk	Growth, cell walls, biomechanics, water relations, pathogen resistance
Turner, John	University of East Anglia	UK	j.g.turner@uea.ac.uk	Jasmonate, stress, cell wall, signalling, disease
Turner, Simon	University of Manchester	UK	simon.turner@manchester.ac.uk	Arabidopsis, genetics, cellulose, cell wall, transcription, metabolism
Webb, Alex	Cambridge University	UK	aarw2@cam.ac.uk	Signalling, calcium, network modelling, circadian, physiology
Woodward, Ian	University of Sheffield	UK	f.i.woodward@sheffield.ac.uk	Climate change, carbon dioxide, stomata, vegetation, productivity
Young, Jayne	University of Sheffield	UK	j.young@sheffield.ac.uk	Organizer